24.

Obstetrics and Animal Experimentation

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ENGLAND

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"The humanity which would prevent human suffering is a deeper and truer humanity than the humanity which would save pain or death to animals."—*Charles W. Eliot.*

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Obstetrics and Animal Experimentation

ROYAL COLLEGE OF SURGEONS OF ENGLAND

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OBSTETRICS AND ANIMAL EXPERIMENTATION

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[EDITORIAL NOTE:—Dr. Williams is well fitted to speak on the above subject. He is one of the fourth generation of a family of physicians, who have been continuously engaged in the practice of medicine since 1770. He is dean of the Johns Hopkins Medical School and has been associated with it and the Johns Hopkins Hospital since its opening as assistant in gynecology, associate, associate professor and professor of obstetrics. He is a member of the Board of Charities of Baltimore City, a member of the Executive Committee of the Federated Charities, Baltimore, and holds membership in many prominent American and foreign obstetric and gynecologic societies. In connection with the work of the Board of Charities he has been especially interested in the hospital care of the sick poor of Baltimore, and has been instrumental in inaugurating the beginning of a well-equipped city hospital, which will be devoted to the care of the poor and to medical teaching.]

Unfortunately, the relation between animal experimentation and obstetrics appears at first sight to be less direct and striking than in many other branches of medicine. Nevertheless, I consider that it can be demonstrated beyond peradventure that the greater part of the advances made during the past thirty-five years have resulted either directly or indirectly from research of this character.

The chief advances in obstetrics, in which animal experimentation has played a part, may be summarized as follows:

1. The recognition of the bacterial origin of puerperal infection, which has enabled us to prevent and overcome its former terrible mortality.
2. The application of aseptic technic to various obstetrical operations, thereby rendering comparatively harmless many procedures which were formerly murderous.
3. The recognition of the bacterial nature of certain infectious diseases of the newly born child, such as lockjaw and umbilical infections, which enables us to save each year the lives of thousands of infants, which under former conditions would have been lost.
4. The biologic study and standardization of certain drugs, such as ergot, whereby efficient preparations are available for the prevention and control of hemorrhage.
5. The demonstration of the internal secretion of the ovary, which has led to the therapeutic employment of ovarian tissue extracts, and to greatly increased conservatism in operations on the ovaries.
6. Experimental studies concerning the nature of the toxemias of pregnancy.
7. The experimental production of fetal deformities, which has led to a clearer conception of teratology, and the abandonment of the superstitious belief in maternal impressions.

1. THE RECOGNITION OF THE BACTERIAL ORIGIN OF PUERPERAL FEVER

Those not familiar with the older obstetrical literature scarcely realize the extent of the ravages of puerperal infection before the introduction of rigid antiseptic precautions in the conduct of labor, as well as the almost miraculous revolution which has followed their employment.

In this connection, I shall attempt to give some idea of the mortality attending puerperal infection in the past, and of the confusion regarding its nature. Then I shall refer to the part played by animal experimentation in the development of the bacteriology of wound infection and the establishment of aseptic technic, as well as the demonstration of the bacterial nature of puerperal infection, and finally I shall refer briefly to the revolutionary results which have followed the practical application of these principles.

In preantiseptic times puerperal fever ravaged the lying-in hospitals throughout the world, and each year caused the unnecessary death of thousands of women in the best years of life. How great the mortality was can best be appreciated by referring to the results obtained in the various civilized countries of the world, prior to the recognition of the etiologic rôle of the streptococcus.

PUERPERAL FEVER IN FRANCE

LeFort, in his railing accusation against the lying-in hospitals of France, which appeared in 1866, calculated that 30,394 deaths from puerperal fever had occurred in the 888,312 women delivered in the hospitals of Paris up to the year 1864—an incidence of 3.5 per cent., or one death to every 27.2 labors. Moreover, he stated that from 1860 to 1864, inclusive, the mortality in the Maternité of Paris was 12.4 per cent., which in December, 1864, rose to the colossal height of 57 per cent.; while in the Clinique it averaged 14.7 per cent. between the years 1833 and 1864, and on several occasions rose above 20 per cent. On the other hand, the mortality outside of the hospitals was much less, as only one woman perished out of every 212, which indicated that seven-eighths of the hospital deaths were due to conditions prevailing in them.

Such results were not limited to the past century, as Tenon in 1788 reported that the mortality at the Hôtel-Dieu for the fifteen years prior to 1786 was 6.4 per cent., and described almost inconceivable conditions of overcrowding and filth. Other observers described similar conditions. Thus, Charrier recorded a mortality of 7.5 per cent. at the Maternité in 1854, and Depaul one of 5.3 per cent. at the Clinique in 1856. Tarnier in his graduation thesis pointed out that 114 deaths from puerperal fever had occurred at the Maternité during the year 1856, an incidence of 5.1 per cent., as compared with 0.31 per cent. in the portion of the city immediately adjoining it.

Malgaine likewise studied the results in 14,197 and 99,911 women delivered respectively, in the hospitals and in the city of Paris during the years 1861 and 1862, and found a mortality of 8.2 and 0.56 per cent.; while Quinquaud stated that 65 per cent. of all women delivered in the St. Antoine Hospital during the year 1869 were infected. Moreover, Delaunay in his recent history of the Maternité de Paris reports that the average mortality for the ten years ending with 1869 was 10.12 per cent., which rose as high as 18.43 per cent. in 1864.

Naturally, such results could not pass unnoticed, and the subject was frequently brought up for discussion. Thus, following a paper on puerperal fever by Guérard before the Académie de Médecine in 1858, a discussion arose which lasted for five months, which led to no definite conclusions, although participated in by the leading authorities in France. Similar discussions also occurred before the Académie in 1861 and 1862, the Société de Chirurgie in 1866, and the Société médicale des hôpitaux in 1869 and 1870. In all of them the most divergent views were expressed, some speakers holding that puerperal fever was contagious, and others that it was an unavoidable visitation of Providence. All sorts of theories were advanced in explanation of its origin, and it was attributed in turn to the peculiar characteristics of the parturient and puerperal woman, to hospital miasms and to the filthiness, faulty construction and ventilation of the hospitals, but not a word was said concerning the dirty hands of the obstetrician. Every suggestion was tested as soon as made, but still the mortality continued unchecked. Finally, in desperation it was suggested that the old lying-in hospitals be abandoned and be replaced by smaller ones, accommodating only a limited number of women, and that most women be cared for in their own homes or in small institutions conducted by specially appointed midwives. At the end of this period, the results had become so intolerable that it became the prevailing opinion that epidemics could be combated only by closing the lying-in hospitals, and such a drastic remedy was forcefully recommended at the International Congress held at Brussels in 1875.

The prevalence of puerperal fever had become a scandal, and, passing beyond purely medical circles, engaged the earnest attention of the Bureau of Public Assistance, whose able director, Husson, after thoroughly investigating the subject, was forced to admit that he saw no way of coping with it, and said:

> For the past sixty years the combined efforts of the administration and of the chiefs of service of health, have not been able to control the curse of puerperal fever, and up to this time the only palliative means of any effect in opposing the evil has been the momentary evacuation of the infected wards. The figures received from the various services of obstetrics still show a mortality high enough to call forth investigation, and to engage the friends of science and humanity to search

in every possible way by what means it may be possible to arrest the progress of so terrible a malady, which up to the present time has disappointed all calculations.

It is interesting to note that the monumental work of LeFort, whose statistics are quoted above, was undertaken at the instigation of Husson; but, when the report was ready and showed so clearly the glaring conditions in France, the Bureau of Public Assistance would not allow it to be published under its auspices. The following quotation from Hervieux's immense work on puerperal infection, which appeared in 1870, will also serve to indicate the gravity of the situation:

> The puerperal epidemics are to woman what war is to man. Like war they destroy the most healthy, the bravest and the most useful portion of the population; like war they take subjects in the flower of their age and spread terror and desolation throughout the territory which they devastate. It belongs to politics to preserve us from the calamities of war, but to medicine is reserved the task of preventing and doing away with such epidemics.

PUERPERAL FEVER IN GERMANY

Conditions similar to those in France likewise obtained in Germany, but owing to the smaller size of its lying-in hospitals, the epidemics were usually not so extensive. Hirsch, in his handbook of historical-geographical pathology, stated that the death-rate in lying-in hospitals varied from 2 to 4 per cent.; while Winckel, on the basis of 701,322 labors in hospitals and 381,855 in private practice, calculated that the average mortality was 3.4 and 0.6 per cent. respectively.

On behalf of the Berlin Obstetrical Society, Boehr in 1877 undertook to study the mortality from puerperal fever in Prussia, and found that in the sixty years ending with 1875 the appalling number of 363,624 women had died from it in that state alone. Moreover, he calculated that the disease was the cause of 12 per cent. of the total number of deaths occurring in both sexes between the ages 15 and 50 years which increased to 18.58 per cent. between the ages 25 and 30 years. Furthermore, assuming that each marriage would result in 4.2 children, he estimated that every thirtieth married woman in Prussia would eventually fall a victim to it.

Based on Boehr's work, and its own investigations, a committee of the society presented a *Denkschrift* to the minister of education, in which it was stated that many more persons died from puerperal fever than from cholera and small-pox combined, although sixteen epidemics of the former disease had occurred during the period covered by the statistics. For the protection of the public health, it was urged that the disease be made a "notifiable" one, so that steps could be taken to regulate the practice of midwives. Hegar made a similar study of the conditions in Baden and found that 0.732 per cent. of all labors ended fatally, one-half of the total number of deaths being due to puerperal fever.

While such results were bad, they did not compare with the conditions prevailing in the lying-in hospitals. Busch and Seyfert reported a mortality of 2.58 per cent. and of 3.5 per cent. in the clinics of Berlin and Prague, respectively. Carl Braun stated that in 98,902 deliveries in the Vienna clinic, between the years 1839 and 1853, the mortality was 4.6 per cent., which even in the pay department reached 2.9 per cent. Ahlfeld relates that during the year in which he served as intern in the Leipzig clinic, 5 per cent. of the women died from puerperal fever and 47.3 per cent. were seriously sick.

Similar results might be adduced more or less indefinitely, but it will suffice to mention that Feige recorded a mortality of 13 per cent. in the Charité in Berlin in 1861 and 1862. Olshausen one of 3.3 per cent. in Halle for the years 1871–1875, and Hecker one of 1.3 per cent. in Munich for the twenty years ending 1879. The work of Boehr was continued by Ehlers in 1900, who found as the result of aseptic precautions that the mortality in the large cities had been reduced by one-half, but had remained practically unchanged in the country districts.

PUERPERAL FEVER IN GREAT BRITAIN

Epidemics of puerperal fever were reported in the eighteenth century by Hunter, Denman, Hulme, Leake, Kirkland, Clarke, White, Gordon and others, the most extensive being that recorded by White in the Lying-In Hospital of Manchester, where the mortality was 4.1 per cent. between the years 1755 and 1771. Owing to the comparatively small size of the lying-in hospitals of Great Britain, and particularly to the early recognition by English physicians of the contagious nature of puerperal fever and its relation to erysipelas, the epidemics were not so extensive and were less fatal than those on the continent; nevertheless, prior to the antiseptic period the results obtained were very discouraging. Until recently, the Rotunda Hospital in Dublin was the only large lying-in institution in the British Empire, and its results have been recorded by Churchill, Kennedy and Steele. The latter stated that in 198,481 labors, occurring up to the year 1870 the average mortality was 1.39 per cent., which rose to 3.27 per cent. between 1861 and 1870. He also reported that for the twenty-two years preceding and including 1876, the several London lying-in hospitals presented the following mortalities:

	Per cent.
Queen Charlotte Hospital	2.82
British Lying-In Hospital	1.57
General Lying-In Hospital	1.41
City of London Lying-In Hospital	1.35

According to Bristowe and Holmes the mortality in the York Road Hospital for the twenty-four years ending with 1858 was 2.9 per cent., which rose to 26.7 per cent. during the epidemic in 1838; while Florence Nightingale stated that between 1862 and 1865 the mortality in the Kings College lying-in department was 3.3 per cent. and was considered so serious that the service was discontinued.

Some idea of the seriousness with which the condition was regarded was shown by the appearance of an editorial in the *Lancet,* only a few weeks after the appearance of Lister's first article on antiseptic surgery, recommending the closing of all lying-in hospitals. Moreover, Kennedy in 1869 advocated evacuating the Rotunda Hospital in Dublin and delivering the women in tents or shacks scattered throughout its grounds; while Florence Nightingale considered that large lying-in hospitals could never be conducted safely and that their employment for the training of students was incompatible with a low death-rate.

Following a paper by Spencer Wells, the entire question of puerperal infection was thoroughly discussed before the London Obstetrical Society in 1875. All of the prominent obstetricians of the time took part in the discussion, and, while the most divergent views were expressed concerning its nature, the general consensus of opinion was that lying-in hospitals had an inherent mortality which could probably never be overcome.

This feeling is well illustrated by the following quotation from Barnes:

> There is only one secret of safety, and that is to have the woman confined at her own house where she can have her own nurse, who has not been anywhere in the way of infection, and her own medical man who is free from infection. Then the chances are that she will come on favorably and happy. Without that there is no security. The lying-in hospital is not now by any means so serious a matter as it used to be; still it is always like sitting on a volcano; it may explode at any moment.

Furthermore, the general feeling of hoplessness was well expressed by Duncan, in his monograph on "The Mortality of Childbed," when he said:

> The disease may have its ravages restricted, but it is yet to be shown that it can be altogether prevented. It is in truth as little preventable as any disease in the nosology, or any crime in the statute-book. It is possibly preventable, but it has certainly never been prevented.

Even after the introduction of antiseptic methods. the views as to the undesirability of lying-in hospitals continued to persist in England; and as late as 1885 one of the sections in Playfair's text-book on midwifery was entitled "Should Lying-In Hospitals Be Abolished?" Indeed, the improvement in that country has been less marked than elsewhere, as Cullingworth, after studying the statistics of the Registrar General's office for 1897, stated that the general mortality had shown no decrease, except as compared with the year 1843; while Boxall reported a similar condition of affairs as late as 1905.

PUERPERAL FEVER IN THE UNITED STATES

That the United States was not spared in this regard is shown by the fact that Hodge reported a mortality of 5.6 per cent. in the Pennsylvania Hospital for the thirty years preceeding 1833. Lusk observed an epidemic in the Bellevue Hospital in 1872 with a mortality of 18 per cent., which led to the removal of the department to Blackwell's Island. But even there the infection continued until after the introduction of antiseptic methods. Similar results were observed in the New York Maternity Hospital, where Garrigues noted a mortality of 4.17 per cent. for the years 1875–

1883, which in the latter year, just prior to the introduction of antiseptic methods, rose to 7.17 per cent.

PUERPERAL FEVER IN SCANDINAVIA

Even Scandinavia was not spared, and Stadfeldt reported the following results from the Copenhagen lying-in hospital: 1822-1843, 5.3 per cent.; 1850-1864, 4.1 per cent.; 1865-1874, 2 per cent. Similar conditions prevailed in Stockholm, and according to Netzel the average mortality was 4.5 per cent. in 45,863 labors occurring in the lying-in hospital during the 102 years ending 1877, and in four years it rose as high as 13 per cent.

VIEWS CONCERNING THE NATURE OF PUERPERAL FEVER

Sedillot stated in 1817 that puerperal fever was not a distinct disease, but rather an ordinary infection, which was modified by the puerperal state. It required, however, nearly seventy years before this doctrine became generally accepted.

The infectious nature of puerperal fever was first clearly emphasized by Gordon of Aberdeen, who based his conviction on seventy-seven cases observed during an epidemic in Aberdeen between the years 1789 and 1792. Among other things, in his forceful monograph, he wrote:

"It is a disagreeable declaration for me to mention that I myself was the means of carrying the infection to a great number of women"; and, in another place, "Fresh air and cleanliness are not sufficient for the destruction of the contagion, which can only be effected by fire and smoke."

Notwithstanding these clear-cut teachings, and the conclusive evidence which Gordon adduced in their support, the medical world was but little affected, and it was not until after the introduction of Listerian methods that such ideas became generally accepted. Similar views were forcibly and eloquently expressed in 1843 by Oliver Wendell Holmes in his monograph on "The Contagiousness of Puerperal Fever," which was reprinted with additions in 1855 under the title "Puerperal Fever as a Private Pestilence." His teachings, however, were opposed by Hodge and Meigs, the leading obstetricians of the day, and, while impressing many practitioners with the necessity of temporarily abstaining from obstetric work when several fever cases had occurred in their practice, they had no effect on the results obtained in lying-in hospitals. Kneeland expressed similar views in 1847, which met with the same fate.

The most important contribution to this aspect of the subject was made by Semmelweis in 1847, who, after carefully studying the causes underlying the horrible mortality in the lying-in hospital of Vienna, came to the conclusion that the disease was identical with wound infection, and was due to the contamination of patients by hands soiled by contact with autopsy material or wound secretions. Furthermore, he thought that its propagation could be checked by washing the hands in a solution of chlorinated lime, by which means he was able to reduce the mortality from 11.4 to 1.27 per cent.

Semmelweis' views concerning the nature and causation of puerperal fever were perfectly clear; and if, in the following quotation, one substitutes the words "pyogenic bacteria" for "decomposed animal organic material" his conception holds perfectly good at the present time. After stating that he regarded child-bed fever as a resorption fever, he continued:

> The decomposed animal organic material, which when absorbed causes child-bed fever, is in the vast majority of cases brought to the individual from without. These are the cases which represent child-bed fever epidemics, and these are the cases which can be prevented. The carrier of the decomposed animal organic material is the examining finger, the operating hand, bed-clothes, the atmospheric air, sponges, the hands of midwives and nurses which have been in contact with the excreta of seriously sick puerperal women or other ill persons and then handle parturient or recently delivered women. In a word, the carrier of the decomposed animal organic material is anything which has been contaminated by decomposed animal organic material and then comes in contact with the genitals of the individual. The area from which the decomposed animal organic material is absorbed is the internal surface of the uterus, extending upward from the internal os. As the result of pregnancy this has been robbed of its mucous membrane, and accordingly presents a surface which is unusually adapted for absorption.

His original observations were brought to the attention of the profession by Hebra in 1847, while his entire doctrine was laid down in his book, "Die Aetiologie.

der Begriff und die Prophylaxis des Kindbettfiebers," which appeared in 1861. In spite of his clear-cut views, his teachings were opposed by the leading authorities of Germany and France, and he died a disappointed man. He nevertheless prophesied that his views would eventually be universally accepted, and, in a postscript to his great work, wrote:

> But should it not be vouchsafed me, which I hope God may prevent, to see this happy time with my own eyes, nevertheless the conviction that such a time must inevitably come sooner or later will cheer me in my dying hour.

Almost simultaneously with Semmelweis, Simpson insisted on the contagious nature of the disease and its identity with ordinary wound infection. More or less similar views were also expressed by Tarnier in 1856 and by Trousseau in 1858; but it was necessary for many years to elapse before they were accepted by the general mass of the profession.

The discrepancy of opinion on the subject is well illustrated in connection with the proposal to erect a new lying-in hospital in Prague, when the Bohemian Landtag submitted to a commission composed of Oppolzer, Rokitansky, Skoda, Virchow, Lange, Schwarz, Hecker and Loeschner, a series of questions concerning the contagiousness of puerperal fever and the advisability of replacing large lying-in hospitals by small ones. Without hesitation, the first three members of the commission replied that the disease was infectious and its spread could be prevented by proper precautions; whereas, the remaining members held various views, but all agreed that large lying-in hospitals were highly dangerous and that the disease could be combated only by greatly limiting the number of women cared for in such institutions.

A similar divergence of opinion continued until after 1875, when the discoveries of Lister and the bacterial origin of puerperal fever first began to be accepted. Prior to that time, the condition was generally considered as unavoidable, and was attributed to cosmic, atmospheric or telluric influences, to the genius epidemicus, imperfect ventilation and all sorts of other conditions; but, with the exception of a few far-seeing men, no one believed that it could be communicated from one patient to another by means of a dirty finger.

The teachings of Lister were introduced into France in 1875 by Championnière and Budin, and were popularized in Germany by a personal tour. Ahlfeld has given an interesting reminiscence of Lister's visit to Leipsic at that time, and has preserved a verse sung in his honor.

Just sind es jetzt fünf Jahre her,
Da drang die Kunde übers Meer;
Es lebt ein Mann in Edinburg,
Das sei ein eigener Chirurg,
In Karbolnebel eingehüllt,
Der rings die Luft mit Dünsten füllt,
Betriebe er mit aller Macht,
Die niedere Bakterienjagd . . .

Prior to that time only a few voices were raised in support of the bacterial nature of puerperal fever, and Lee and Sir Spencer Wells were practically alone in England in advocating it. Indeed, such views did not begin to receive general acceptance until after Pasteur had cultivated the streptococcus and demonstrated it before the Académie de Médecine de Paris, in March, 1879.

It is interesting to recall the fact that the demonstration was preceded by a paper by Hervieux, in which he said:

> "I lay down the principle that the inferior organisms as yet known, vibrions, bacteria, batonnets and moving bodies, cannot possibly explain the production of puerperal septicemia," and concluded, "but I must confess that I have a terrible fear, a fear from which I am not able to rid myself, and which the academy will understand; and that is that I shall die before any one will have discovered that vibrion."

Immediately afterwards Pasteur arose and drew on the blackboard several chains of little dots, which he stated he had every reason to believe were its actual cause. This was the beginning, but many years of persistent investigation were required before the bacterial nature of puerperal infection was universally recognized, and, even as late as 1886, Credé in Germany and Munde in this country were doubtful whether sufficient proof had been adduced in its support.

THE DEVELOPMENT OF BACTERIOLOGY; AND RECOGNITION OF BACTERIAL ORIGIN OF PUERPERAL INFECTION

This is not the place to trace the history of the development of bacteriology in general, or even its application to wound infection. As far as I can learn, the relation of bacteria to infectious diseases, and the necessity of recourse to animal experimentation for its demonstration, was first clearly expressed by Henle in 1840. He prophesied that the "contagium" in infectious diseases must be a living organism, and laid down the following criteria, which must be fulfilled in order to prove such a relationship:

1. The constant presence of one and the same microorganism.
2. Its isolation.
3. The experimental study of the same by animal experimentation.

Following this, the development of bacteriology as applied to medicine was comparatively slow, and it was not until after the work of Pasteur on putrefaction, and the application of his ideas to surgery by Lister, that very considerable advances were made. Indeed, it may be said that extensive development along these lines was not possible until after Koch, by the discovery of solid culture media, had put into our hands a convenient method of isolating and cultivating bacteria. Almost immediately following this invention, the various bacteria concerned in ordinary wound infection were isolated and their pathogenic action demonstrated experimentally on animals. Aside from Pasteur and Koch, the greater part of this work was done by Ogston, Rosenbach, Passet, Garre and Fehleisen, and so convincing was their demonstration, that the information concerning the pyogenic cocci given in Baumgarten's "Handbuch der pathologischen Mycologie" in 1887 is almost as satisfactory as that available at the present time. Moreover, between the years 1884 and 1889, the work of Carle and Rattone, Nicolaier and Kitasato resulted in the isolation of the tetanus bacillus, and the conclusive experimental demonstration of its pathogenic action.

All of these discoveries were based on animal experimentation, and indeed it may be said that none of the important advances in bacteriology would have been possible without its aid. Occasionally, enthusiastic investigators, such as Bumm, Garre, Bockhart and Fehleisen, made experiments on their own persons, and thereby still further convinced themselves of the pathogenic properties of certain pyogenic bacteria.

Following the recognition of the bacteria concerned in the production of wound infection, it became possible to test the efficiency of the various antiseptics recommended for their destruction. It is particularly to Koch that we are indebted for the fundamental contribution to the doctrine of disinfection, and for the demonstration of the great value of bichlorid of mercury. Further investigation, however, gradually materially impaired our faith in the efficacy of antiseptics, and led to the development of aseptic surgery. This resulted, on the one hand, from the demonstration of the deleterious action of disinfectants on the tissues, and on the other, from the recognition of the practical impossibility of rendering the hands absolutely sterile by means of antiseptic solutions. The realization of the latter fact led to the introduction of rubber gloves, which has enabled us to do away with all danger of infection by the hand of the operator, and together with the sterilization of dressings, instruments and suture material by means of steam, has reduced to the lowest possible limits the possibility of the introduction of bacteria into wounds.

All of these advances were based directly on the practical application of bacteriology, and this in turn owed its development solely to animal experimentation. Manninger, after a careful historical review of the development of antiseptic and aseptic surgical technic, makes the same statement, and holds that in no other field have its benefits been so clearly marked as in obstetrics.

As far as I have been able to learn, Semmelweis in 1846 was the first to resort to animal experimentation in the hope of solving the problem of puerperal infection. He introduced into the freshly delivered uterus of animals, uterine discharges and peritoneal exudate from infected women, as well as the exudate from men dead of peritonitis, and in the majority of instances was able to bring about the death of the animal from infection. Animal experiments were also made by Tarnier, Mayrhofer, Coze and Feltz, Quinquand, Orth, Heiberg, Eberth, D'Espine, Kehrer, Karewsky, Miller, Pasteur and Doléris and many other later investigators.

Of these Mayrhofer, Coze and Feltz, Pasteur and Doléris deserve especial mention. The former in 1864 observed bacteria in the interior of the infected uterus.

which he described as vibrions, and by the injection into animals of lochia containing them was able to reproduce the disease. Coze and Feltz in 1869 apparently demonstrated the presence of streptococci in the blood of women dying from puerperal fever, and cultivated them in rudimentary fluid culture media. They also produced death in animals by their innoculation. As has already been mentioned, Pasteur was the first to describe clearly, and to cultivate the streptococcus from cases of puerperal infection, and together with his collaborator Doléris effectively demonstrated its etiologic significance.

Following Pasteur, it has gradually been demonstrated that, while the streptococcus is the organism most usually concerned in the production of fatal puerperal infections, all of the pyogenic bacteria, which play a part in ordinary wound infection, may likewise give rise to them. Scarcely any one who has busied himself with their study has failed to resort to animal experimentation, and none of the recent advances along this line would have been possible without its aid.

Listerian methods were not adopted in gynecology and obstetrics until after 1875, and for the succeeding few years the chief reliance was placed on the free use of phenol for disinfecting the hands and dressings and for use as a spray. Such precautions were soon carried to ridiculous extremes, and at the acme of the antiseptic period it was thought necessary to remove all furniture from the room in which a woman was to be confined, to scrub the walls and floors with a phenol solution and to have a nebulizer spray it on the external genitalia during the second stage of labor. At the same time, disinfection of the hands was slighted, as it was believed that their immersion in a phenol solution for a few moments was sufficient to render them absolutely sterile. As these precautions did not lead to the complete disappearance of puerperal infection, the attempt was made to destroy all bacteria in the birth canal by means of vaginal and intra-uterine douches of phenol solution, or of bichlorid of mercury, after its introduction in 1881. That such practices were not without danger was soon shown by the appearance in the literature of large series of cases in which death occurred from phenol or bichlorid poisoning.

With the gradual development of clearer ideas concerning the process of infection and the limitations of disinfection in general, the employment of antiseptic methods was gradually abandoned and its place taken by the aseptic technic which we now employ, in which less and less importance is attached to chemical disinfection and increasingly more weight laid on absolute subjective and objective cleanliness.

RESULTS FOLLOWING THE EMPLOYMENT OF ANTISEPTIC AND ASEPTIC TECHNIC

Following the introduction of antiseptic methods into obstetrics, there occurred a marked diminution in the death-rate from puerperal infection, which however, was nothing like so great as in the later or aseptic period. Thus, Dohrn analyzed the results obtained in 104,278 women delivered in forty-seven German lying-in institutions between the years 1874 and 1883 inclusive, and found an average mortality of 1.37 per cent. At the beginning of the period it was 1.73 per cent., and became reduced to 0.96 per cent. at its end. Moreover, it is interesting to note that the worst results were obtained in the institutions used for the instruction of students, while the best were in those not employed for teaching purposes, the mortality averaging 1.9 and 0.56 per cent., respectively.

When compared with the mortality of 3 or 4 per cent., which characterized the previous decade, the results were most encouraging; and Dohrn felt that they probably could not be improved on, as he stated that "the mortality in lying-in hospitals will never be lowered for any great length of time to the percentage prevailing in private practice; and, if we estimate the latter at 0.6 to 0.7 per cent., the institutional mortality would still be nearly double as high. The lying-in institutions have to contend with such unfavorable conditions that such results as in private practice would never be permanently possible."

Bar stated that, following the introduction of antiseptic methods in the Maternité of Paris, the mortality fell to 1 per cent. in 1873 and to 0.8 per cent. in 1882: while Tarnier has given a very graphic picture of the conditions in the same hospital. For this purpose he distinguished three periods; namely, from 1858 to 1869, from 1870 to 1880, and from 1881 to 1889, and designating the first as the period of inaction, the second as that of fight against contagion and the third as the antiseptic period, recorded a mortality of 9.31, 2.32 and 1.05 per cent., respectively. On the other hand, at the Clinique where Depaul and Pajot, who did not believe in the bacterial nature of the disease, continued to use the old methods, as many patients died as previously.

With the gradual development of aseptic technic and more rigid precautions for the prevention of infection, better and better results were obtained, so that Mermann in 1907 was able to report a septic mortality of only 0.08 per cent. in 8,700 patients delivered under his supervision in Mannheim. Pinard in 1909 reported a net mortality of 0.15 per cent. in 45,633 deliveries in the Baudelocque Clinic during the eighteen years ending with 1908; while in the same year Markoe recorded a percentage of 0.34 in 60,000 women delivered by the Society of the New York Lying-in Hospital.

At the present time it is safe to say that in well-regulated hospitals the mortality from puerperal infection is less than 0.25 per cent. This is in great contrast with the average mortality of 3 to 4 per cent. observed throughout the world prior to the introduction of antiseptic methods, and means that only one woman now dies as compared with fifteen or twenty formerly. Moreover, the criterion of excellence in lying-in hospitals is now not so much the actual mortality as the morbidity of patients; namely, the percentage in whom the temperature rises to 38 C. or 100.4 F. during the first ten days of the puerperium.

This improvement is astounding, and at the present time it is safe to say that fewer deaths from infection occur in well-regulated lying-in institutions than in private practice, notwithstanding the fact that in the former the patients are freely used for clinical instruction. In this regard Dohrn and Florence Nightingale were poor prophets, as the former stated that such results would never be attained; while the latter held that hospitals could not be rid of puerperal infection as long as they were used for the instruction of students.

This revolution must be attributed to animal experimentation, which made possible the demonstration that definite bacteria are the cause of wound infection, and that one of its varieties—puerperal infection—is due to the introduction of pyogenic bacteria into the birth canal of parturient women, and can be prevented by appropriate means. Of course, it may be urged that far-seeing men, such as Gordon, Holmes, Semmelweis and Tarnier realized the contagious nature of puerperal fever long before bacteriology became a science. They were not, however, able to impress their belief on the profession, and consequently no improvement was observed until the bacterial nature of the disease was clearly demonstrated. Formerly, the obstetrician groped in the dark in his attempt to identify the unknown contagion, if he even believed in its existence; while now we know exactly with what microorganisms we have to deal, and the means to adopt in order to overcome them.

At the present time, puerperal infection is no longer regarded as a visitation of Providence, but is attributed directly to the introduction of bacteria following a "break" in aseptic technic; and, whenever a case occurs in a well-regulated hospital, the director immediately begins to inquire how it happened, and, having found the source, is at once able to put a stop to further spread of the disease.

2. *THE APPLICATION OF ASEPTIC TECHNIC TO OBSTETRIC OPERATIONS*

The same factors which led to the disappearance of puerperal fever from lying-in hospitals and made possible the wonderful advances in general surgery, played an identical part in revolutionizing the results following the various operative procedures in obstetrics.

This is most strikingly illustrated by contrasting the results following Cesarean section and symphyseotomy or pubiotomy during the preantiseptic period and at the present time. Even as late as 1886, Dr. Robert Barnes wrote:

> The Cesarean section occupies a doubtful place between conservative and sacrificial midwifery. It is conservative in its design, in its ambition: it is too often sacrificial in fact. It is resorted to with a feeling akin to despair for the fate of the mother, which is scarcely tempered by the hope of rescuing the child. It is looked upon by the great majority of obstetricians as a last desperate resource, as the most forcible example of that kind of surgery which John Hunter regarded as the reproach of surgeons, being a confession that their art was baffled.

From 1787 until 1879, when Tarnier reported his first operation under antiseptic precautions, not a single successful Cesarean section had been performed in Paris; while Lusk, in the early eighties, was the first successful operator in New York. Dr. Robert T. Harris stated that in the forty Cesarean sections performed in the United States up to the year 1860, the mortality was 52 per cent.; while Radford estimated it at 84 per cent. in the 100 operations performed in England up to that time. Indeed, as late as 1887, Harris stated that Cesarean section could be performed more safely by the horn of an infuriated bull than by the most accomplished surgeon in the best-equipped hospital in America. In support of this statement, he collected from the literature nine instances in which the abdomen of pregnant women had been ripped open by the horn of an infuriated bull, with five recoveries; whereas, only two mothers had survived the eleven Cesarean sections which had been performed in New York up to that time.

This horrible mortality was revolutionized by two factors: namely, the development of antiseptic surgery, and the description by Sänger in 1882 of a proper technic for suturing the uterine incision. The results following their adoption were so striking that Caruso was able to report that in 135 operations performed between the years 1882 and 1888, the mortality had been reduced to 25.56 per cent. Following the employment of more rigid technic and the proper selection of cases, this was gradually lowered, so that at the present time Cesarean section is undertaken by competent operators without hesitation, and gives most satisfactory results, as is indicated by the following figures: Thus, Bürger, in 1908, reported a gross mortality of 3.4 per cent. in 116 consecutive operations performed in Schauta's clinic, and Markoe one of 6.45 per cent. in 124 uncomplicated cases in the New York Lying-in Hospital. Moreover, Leopold has just recorded a gross and a net mortality of 6.2 and 3.3 per cent., respectively, in 303 operations performed in the Dresden clinic, and states that the last seventy operations were uniformly successful. In this country, Reynolds has thirty consecutive successful operations to his credit, and has pointed out that the danger is very slight if the operation is performed early, but increases rapidly with each hour of labor, as is shown by the following analysis:

	Per cent.
82 operations before onset of labor, mortality	1.2
158 operations early in labor, mortality	3
49 operations late in labor, mortality	12

In view of such results, one may say that the mortality of Cesarean section, performed either in the last weeks of pregnancy or at the very beginning of labor, should not exceed that of ordinary gynecologic laparotomies, which is between 1 and 2 per cent. This striking revolution is due entirely to the development of aseptic surgical technic and to the restriction of the operation to uninfected women, who have not been subjected to the exhaustion incident to prolonged labor.

Exactly the same story can be told concerning symphyseotomy and pubiotomy. The former was first performed in 1777 by Sigault, and immediately afterward enjoyed a short-lived popularity, but soon gave such discouraging results that it was abandoned. Harris was able to collect reports of 70 cases up to 1858, with a maternal and a fetal mortality of 37 and 67 per cent., respectively.

The operation was resuscitated in Naples shortly afterward, and between 1866 and 1880, fifty operations were done, with a maternal mortality of 20 per cent. Following the introduction of antiseptic technic, it came into more general use, and Neugebauer in 1893 calculated that the mortality had fallen to 11.1 per cent.; while Mayer in 1908 stated that it had become still further reduced, but was still as high as 6 per cent. In view of the relatively high death-rate, and the more satisfactory results following Cesarean section, the operation gradually fell into desuetude, but was resuscitated again in 1897 under the form of pubiotomy.

Owing to the further development of aseptic technic, and the exact recognition of the character of cases susceptible to it, the mortality of pubiotomy has been kept within low limits, so that in May, 1910, I was able to collect from the literature reports of 518 operations performed by less than twenty operators, with a gross mortality of 1.9 per cent. In my clinic thirty odd pubiotomies have been done with no maternal deaths, while Roth has just reported eighty-five operations from Leopold's clinic with two deaths.

Similar improvement has occurred in the results following all other obstetric operations—forceps, version, induction of labor, *accouchement forcé,* etc. Unfortunately, it must be admitted that owing to the comparative immunity from danger there has developed a tendency on the part of many to resort unnecessarily to operative procedures, when Nature alone would have brought about a happy termination. Notwithstanding such tendencies, however, the general result is most creditable, and stands out in wonderful contrast to that of the past, and has each year been the means of saving the lives and diminishing the sufferings of thousands of women.

In this connection, one cannot reiterate too strongly that all of these advances must be traced back to the same cause, namely, the development of bacteriology and of aseptic surgical technic, both of which in turn are entirely dependent on the employment of animal experimentation.

3. *THE RECOGNITION OF THE BACTERIAL NATURE OF CERTAIN INFECTIOUS DISEASES IN THE NEW-BORN CHILD*

In times past, probably the most important disease of this group, occurring in lying-in hospitals, was the so-called puerperal fever of the new-born child. This condition, which was studied particularly by Schindler, Trousseau, Lorain, Hecker and Bühl, Müller and others, occurred particularly when the hospitals were ravaged by puerperal fever, and was due to the infection of the child during labor, or shortly afterward. In the first case, the amniotic fluid became infected during the course of a prolonged labor with concomitant infection of the air passages of the child with subsequent development of bronchopneumonia; while in the latter case, infection occurred through the stump of the umbilical cord. In either event, the disease was extremely fatal and only a small proportion of the infected children escaped, while autopsy showed one or more of the protean manifestations of wound infection; especially, bronchopneumonia, pleurisy, peritonitis, meningitis, erysipelas, pyemia or general septicemia.

Some idea of its incidence may be gained from the fact that a mortality of 7.62 per cent. was observed in the 18,329 children delivered in the Vienna Hospital prior to the work of Semmelweis. Following the employment of the precautions against puerperal fever which he recommended, the fetal death-rate was so markedly reduced that Bednar, who had charge of the Foundling Asylum, stated "that the disease of the children [blood sepsis] had almost entirely disappeared in consequence." Lorain noted a similar connection in the Maternité of Paris and reported that in 2,567 labors occurring during the year 1854, 5.7 per cent of the mothers and 7.5 per cent. of the children were lost, and the high mortality continued until antiseptic precautions were introduced by Tarnier. Hugenberger, likewise, estimated that the average fetal mortality in the St. Petersburg Hospital was 2.6 per cent., which rose as high as 14 per cent. during puerperal fever epidemics; while Hecker and Bühl observed an even higher death rate.

At the present time this condition is observed but rarely, and then only in the case of women who are admitted to the hospital already infected, when the bacteria contained in the amniotic fluid gain access to the child and give rise to infection.

As long as epidemics of so-called fetal puerperal fever occurred, comparatively little attention was paid to the actual mode of infection, but with the subsidence of the disease, the question was more carefully studied. It was then found that the portal of entry was usually through the stump of the umbilical cord, and this type of infection persisted for several years after puerperal fever had practically disappeared from lying-in hospitals.

Occasionally it caused a terrible mortality, and Paquy refers to the experience of Meynet, who lost 17 per cent. of the children cared for in a crêche in Lyons. Moreover, Runge stated that he had observed a mortality of 4 per cent. in Strassburg, as well as nineteen deaths in the Charité in Berlin during the first six months of 1880. His investigations showed that the umbilical arteries were usually involved, while infection occurred only exceptionally through the vein.

Following the introduction of antiseptic methods of caring for the stump of the umbilical cord, this variety of infection rapidly disappeared, so that at present in well-regulated hospitals it occurs only once in many hundred cases. At the same time, owing to the faulty technic, so often observed in this regard, it still occurs too frequently, and should always be suspected whenever a child dies without well-marked symptoms indicative of some definite disease, when autopsy will usually show the umbilical arteries distended by suppurating thrombi, which have given rise to peritonitis or a general systemic infection. We now hold that the condition always results from bacterial invasion, which is usually streptococcic in character; and we are forced to attribute the great diminution in its occurrence to the recognition of its true nature, which was made possible only by the development of bacteriology, which is based on animal experimentation.

Formerly, large numbers of new-born children died each year from tetanus, and Collins stated that during his mastership at the Rotunda in Dublin, one-fifth of all children, dying within the first fortnight after delivery, perished from it. He also referred to the epidemics observed during the mastership of Dr. Clarke, who said "At the conclusion of the year 1782, of 17,650 infants born alive in the hospital, 2,944 died within the first fortnight, and nineteen out of twenty of these died of nine-day fits." This indicates a total fetal mortality of 16.6 per cent., of which 95 per cent. was due to tetanus. This epidemic was held in check by the greatest attention to ventilation and cleanliness, but that the disease was not entirely eradicated is shown by the experience of Collins forty or fifty years later.

Similar epidemics have also been noted in other parts of the world, one of the most remarkable having occurred in the Island of St. Kilda, and was described by Mitchell in 1865. In this epidemic, 67.2 per cent. of all new-born children died, and the horrible death-rate continued until antiseptic methods of caring for the cord were introduced, when Turner reported that dusting the stump with iodoform had led to its complete disappearance. Until comparatively recently, the negro race in the South was often decimated by tetanus neonatorum, and the extent of its ravages may be gained from the following quotation from Grier:

> We have known more than one instance in which, of the births for one year, one-half became the victims of this disease, and that, too, in spite of the utmost watchfulness and care on the part of both planter and physician. Other places are more fortunate, but all suffer more or less, and the planter who

escapes a year without having to record a case of trismus nascentium may congratulate himself as being more favored than his neighbors, and prepare himself for his own allotment, which is surely and speedily to arrive.

Similar conditions likewise obtained in Jamaica, and as early as 1835 Maxwell reported:

> From observations I have made for a series of years, I found that the depopulating influence of trismus neonatorum was not less than 25 per cent. It scarcely has a parallel on the bills of mortality.

Unfortunately, the same condition still prevails, as Pescay recorded identical results in 1900. How seriously the disease was formerly regarded is shown by the fact that the 1889 edition of Dr. J. Lewis Smith's textbook on diseases of children contained a chapter of twenty-one pages on the subject.

Prior to the isolation of the tetanus bacillus, the condition was attributed to filth and impure air, but with the recognition of its specific cause and the employment of aseptic methods in the treatment of the umbilical cord, it has practically disappeared, and I have never encountered a case in more than 10,000 newly-born children under my supervision. This advance, just as all the others, to which I have referred, must be attributed solely to the employment of animal experimentation, for without its aid the tetanus bacillus could not have been isolated, nor its characteristic pathogenic properties demonstrated.

4. *THE BIOLOGIC TESTING OF ERGOT*

This drug, which is now so freely employed throughout the civilized world for the control of postpartum hemorrhage by the stimulation of uterine contractions, was first described medically by Dr. John Stearns of Waterford, N. Y., in 1808; while we owe the first dissertation on its physiologic action to Prescott of Boston in 1822. Following this, its complicated constitution has given rise to almost countless investigations, and pharmacologists are not yet in agreement concerning its active principles. Some idea of the amount of work done on the subject may be gained from the fact that Grünfeld, in his study, which appeared in 1892, required fourteen pages arranged in double column to contain a list of the publications of the previous twenty-five years.

Some of the most important contributions to the action of the drug we owe to Kobert, Jacoby, Grünfeld, Barger and Dale. Ever since its employment for medicinal purposes very conflicting statements have been made concerning its active principles and physiologic action, and it was not until after the careful studies of Grünfeld that the cause for the discrepancy was recognized. He found that the powdered drug rapidly lost its medicinal properties; and while a certain preparation might be very potent when first prepared, it so rapidly deteriorated as to be practically without physiologic effect after being kept for four or five months. The recognition of this fact led to the necessity of devising some method for testing the physiologic activity of the various preparations of ergot before putting them on the market.

Unfortunately, no method of chemical analysis or assay has as yet been devised to enable manufacturing chemists or physiologists to determine the value of a given preparation, so resort was necessarily had to biologic or physiologic tests for the purpose. From the earliest times it had been noted that an efficient preparation would lead to marked bluing, and eventually to gangrene of the comb and wattles of the rooster; although later investigations tended to show that such a result was not necessarily an index of its action on the uterus, as it had been demonstrated that the gangrene-producing properties were quite independent of those causing uterine contraction. Consequently, other modes of investigation became necessary. Kurdinowski determined its physiologic activity by testing its effect on the isolated uterus, Kehrer, instead, used thin slices from the uterus of freshly killed pregnant animals, while Cronin and Henderson studied in animals its effect on the blood-pressure.

According to Crawford, most manufacturing chemists at the present time test its efficiency on the cock's comb and wattles; although he states that it would be preferable to employ the living uterus, as recommended by Kurdinowski and Kehrer. In any event the manufacturing chemist must resort to some such form of animal experimentation in testing every specimen of ergot which he uses for the manufacture of the preparations sold to the public; and that means that no woman can take ergot for the control of hemorrhage without being the recipient of at least one of the advantages which has been gained from animal experimentation.

5. *THE DEMONSTRATION OF THE INTERNAL SECRETION OF THE OVARIES*

Although the atrophic changes occurring in the internal genitalia following the menopause, or the operative removal of the ovaries, were long ago recognized, the possibility that they were a manifestation of the disappearance of an internal secretion, formerly elaborated in those organs, was not suspected until after the appearance of Brown-Séquard's suggestive article on the subject.

As long as such a supposition was not supported by facts capable of demonstration, it was not possible to be sure of its correctness, or to deny that the changes in question were neurotic in origin. The experimental work of Knauer, Gregoriff, Mandl and Bürger, Marshall and others, however, conclusively demonstrated that the ovaries elaborate a definite secretion, which serves to regulate the nutrition of the internal genitalia, as well as to exert a definite effect on the entire organism. Moreover, it was clearly shown that the organs could be removed from their usual site and transplanted to other distant portions of the body, and still prevent the degenerative changes which usually follow their removal. As all nervous connections had been severed at the time of operation, it was evident that the only manner in which such an influence could be exerted was by means of an internal secretion, which gained access to the blood-current.

Other experiments showed that the transplanted ovaries functioned perfectly, and if implanted in a suitable location, produced ova which could be fertilized. Such findings were not merely of scientific interest, but possessed a distinctly practical bearing in that they suggested the possibility of transplanting the ovaries in human beings, as well as the employment of ovarian tissue extract in the treatment of various conditions resulting from imperfect ovarian secretion, more particularly the distressing symptoms which frequently accompany the menopause or follow the removal of the ovaries. Not a few operators, when obliged to remove both tubes and ovaries on account of disease, have implanted healthy portions of the latter on the uterus or broad ligaments, in order to prevent the occurrence of an artificial menopause in young women. Less frequently, the ovaries of one woman have been implanted into another, in the hope of reestablishing the menstrual function, or even making possible the occurrence of pregnancy. The former result has been attained in numerous instances, while the latter has resulted successfully in at least two cases. Those who are interested in the subject are referred for details to Martin's article which contains full references to the literature up to 1908.

Fraenkel, in 1903 and 1910, published two important contributions on the function of the ovaries, which were based entirely on animal experimentation. He apparently showed that the corpus luteum should be regarded as a temporary gland which produces an internal secretion, whose function, at least in part, is to bring about the changes in the internal genitalia necessary to permit the implantation of the fertilized ovum. Furthermore, his experiments rendered it probable that the continuance of the secretion was essential for the preservation of pregnancy during its early periods, but was not necessary later; and thus afforded an explanation for the clinical observation that removal of the ovaries early in pregnancy is usually followed by abortion, whereas their removal later has no effect.

His work also suggested a possible explanation for the not infrequent lack of success in the therapeutic application of ovarian extract, since, if its action were solely due to the presence of corpus luteum tissue, efficiency could not be expected if the preparation consisted only of ordinary ovarian stroma. For this reason, he recommended that in future the so-called ovarian tissue tablets be made exclusively from corpora lutea, and not, as formerly, from the entire substance of the ovary; and clinical reports seem to indicate that his premises were correct.

6. *EXPERIMENTAL STUDIES CONCERNING THE NATURE OF THE TOXEMIAS OF PREGNANCY*

Up to twenty years ago our ideas concerning the nature and etiology of eclampsia were but little clearer than in 1843, when Lever first described the presence of albumin in the urine of eclamptic women, and held on that account that it was merely a variety of nephritis.

Following the experiments of Rivière in 1888, and those of Tarnier and Chamberlent a few years later, in which it was apparently shown that the toxicity of the urine of eclamptic women was greatly decreased for experimental animals, while that of the blood-serum was markedly augmented, the belief gained ground that the condition was toxemic in character, and was due to the retention within the organism of certain substances which were ordinarily excreted through the kidneys. Following these observations, the experimental study of eclampsia has occupied the attention of large numbers of investigators, and although the subject has not yet been thoroughly elucidated, the conviction is growing stronger and stronger each year that the disease is a toxemia, which is in some way dependent on the pregnancy, and in all probability connected with abnormal processes either within the body of the fetus or placenta.

It would carry us too far afield to attempt even to enumerate those who have taken part in such investigations, but the contributions of Volhard, Veit, Hofbauer, Lichtenstein, Freund, and Thies deserve especial mention. Moreover, we might refer, in this connection, to the fact that it is only by means of animal experimentation that we have learned the part which the secretion of the thyroid gland plays in regulating the metabolism of pregnancy.

Although none of these experimental investigations have entirely cleared up the etiology of the affection, they have nevertheless served to impress on us its toxemic nature, and have taught us that the treatment *par excellence* consists in the prompt evacuation of the uterus. Moreover, I consider that if the matter is ever to be settled, it can only be accomplished by the aid of animal and biochemical experimentation.

7. *THE EXPERIMENTAL PRODUCTION OF FETAL DEFORMITIES*

If it is permissible to designate as animal experimentation the various procedures to which the fertilized eggs and the developing embryos of various animals are subjected for the purpose of producing anomalies of development, we can point to a field which has not only markedly advanced our knowledge concerning the normal mechanism of growth and the mode of production of monstrosities, but one which is destined to add greatly to the comfort of the human race.

In times past, the birth of monsters or of children afflicted with congenital deformities was attributed to the anger of the gods, to witchcraft or to some malign influence to which the pregnant woman had been subjected. With the advance of knowledge and the passing of superstition, such views gradually disappeared; but, on the other hand there is scarcely a woman in America at the present time, who does not firmly believe in the doctrine of maternal impressions, and who, in case of the birth of a monstrous or deformed child, will not attempt to trace its origin to some unpleasant sight or experience to which she had been exposed during pregnancy.

Such a belief is not limited to women, but is likewise shared by most medical men in this country, as is shown by the fact that as late as 1889 Keating's "Encyclopedia of Diseases of Children" contained a long article in its favor. Moreover, not a few works on obstetrics direct that the pregnant woman should be guarded from unpleasant sights of all kinds.

Persistence in the belief in maternal impressions is each year a source of great unhappiness to thousands of women, who, after some trivial occurrence, such as seeing a mouse or a rabbit, are convinced that their child will be "mouse-marked" or hare-lipped in consequence, and who do not dismiss their fears until a perfectly normal and well-formed child has been born. Indeed, I feel that I am safe in stating that no one who has not considerable experience with pregnant women can appreciate the extent of the suffering and dread resulting from this superstitition.

The new science of experimental embryology and teratology has shown clearly that such an occurrence is impossible, as in the vast majority of cases, the changes which were attributed to it developed in the earliest periods of pregnancy, whereas the "maternal impression" to which a given deformity was attributed did not occur until a much later date.

Geoffroy Saint-Hilaire, Allen Thompson and Féré were the first investigators to attempt the production of deformities by subjecting the developing egg to various conditions, but it is only within the last twenty-five years that the matter has seriously engaged the attention of scientific men. During this period, however, the work of Pflüger, Dareste, Roux and Born has put the subject on a scientific basis, as they have shown beyond question that pricking certain portions of the segmenting ovum with a needle, encircling it with a ligature, or subjecting it to certain chemical influences, will inevitably be followed by definite deformities, and they were enabled in this way to produce at will, not only single, but double monsters of the most varied type.

Further research along these lines has been particularly prolific in this country, and the investigations of Loeb, Morgan, Wilson, Bardeen, Harrison, Stockard and many other, has led to most astounding results, which have revolutionized our ideas of teratology. These investigators have shown beyond peradventure that practically all of the deformities with which we meet at the time of labor can be produced at will by subjecting the early ovum or embryo to various procedures. Thus, it is possible to produce spina bifida, cyclops, headless or double monsters, as well as those lacking extremities or having accessory ones, merely by changing the experimental conditions.

As the result of these investigations, it has been definitely proved that, with the exception of certain well-marked hereditary deformities, the great majority of monsters are the result of some interference with the normal growth of the ovum in the days immediately following conception, and not to later influences. Moreover, Mall in a study of four hundred early human abortions found that 38 per cent of them were pathologic, and that many presented deformities which were inconsistent with further life. He estimates that in about 7 per cent. of all pregnancies the ovum is abnormal, and as the changes began in the early weeks it is manifest that "impressions" occurring at a later period of pregnancy could have no part in their production.

Indeed, at the present time the evidence available seems to indicate that the entire doctrine of maternal impressions is a superstition which will sooner or later entirely disappear, and this result will be hastened as the work of the experimental teratologist becomes generally known.

CONCLUSION

In conclusion, it may be said that while the benefits which obstetrics have derived from animal experimentation are not immediately apparent, they are nevertheless very real, and have led to revolutions in obstetric practice and to results which are but little realized by the general public. I think that I am safe in asserting that had animal experimentation led to nothing more than the discovery of the bacterial nature of puerperal fever, whereby a means was provided for doing away with its former hideous mortality, it would abundantly justify the sacrifice of all the animals which have thus far been used for experimental purposes. Think of the millions of lives which have been saved, if we accept Boehr's calculation, that formerly every thirtieth married woman has inevitably doomed to perish from puerperal infection. Fortunately, this is not the only benefit even in obstetrics, which can be ascribed to animal experimentation. as the increased security following operations and the marked decrease in the mortality of new-born children are equally attributable to it. Indeed, it may be truthfully said that every time a physician cleanses his hands preparatory to attending a woman in labor, he is rendering a tribute to animal experimentation; although unfortunately, the world at large, which benefits from it, does not recognize its significance. I feel that there is every reason to expect that animal experimentation will play as large a part in developing our ideas in the future as in the past, and I confidently believe that the problem of eclampsia and the other toxemias of pregnancy, as well as the cause of labor and all that that implies, will eventually be solved by its means.

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